ABSTRACTS :

PLASMA LIPIDS IN PATIENTS WITH TYPE I DIABETES MELLITUS

Semenkorich CF, Ostlund RE, Schechtman KB

Arch. Intern. Med. 1989, 149 : 51-56

Abstract

Plasma lipids and hemoglobin A_1 (Hb A_1) were measured in 544 Type I diabetic patients. Hb A_1 was positively correlated with the levels of total plasma cholesterol, total triglycerides (Tg) and low density lipoprotein (LDL) cholesterol and negatively correlated with the level HDL cholesterol in the entire biracial group. These relationships between plasma lipids and Hb A_1 were not present in black woman. In the white diabetic population, a reduction in Hb A_1 of one percentage point was statistically associated with a decrease of 0.1 to 0.17 mmol/L in total plasma cholesterol, a decrease of 0.10 to 0.13 mmol/L in LDL cholesterol, a decrease of 0.10 to 0.13 mmol/L in LDL cholesterol, and a reduction of 0.12 to 0.14 mmol/L in Tg. These findings suggest that race and gender are important determinants of of the response of plasma lipids to glucose control in Type I DM.

Comments

Atherosclerosis is the most common complication of diabetes and lipoproteins arc strongly associated with atherosclerotic process. Abnormal lipoprotein values are commonly observed among patients with type I diabetes mellitus. Total plasma cholesterol, LDL cholesterol and Tg values are higher in diabetic patients with poor metabolic control- Hb A_1 as the measure of glycaemic control was best correlated with lipid values. Lower Hb A_1 was associated with significant lower cholesterol, VLDL and LDL cholesterol, coronary artery disease risk is decreased by 2%. Thus tight glycemic control in diabetics should result in prevention of long term complications of diabetes. This potential benefit of tight glycaemic control must also be weighed against appreciable frequency to hypoglycaemia. These findings were not observed in black women. Hb A_1 and lipoproteins relation is required to be studied in Aryans, Dravidians and sub-Himalayan races, and in both sexes before race and genes are considered as determinnants of the response of lipoproteins to glycaemic control in type I DM.

CLINICAL TRIALS WITH GUGULIPID — A NEW HYPOLIPIDAEMIG AGENT

Nityanand S, Srivastava JS, Asthana OP

JAPI, 1989, 37 : 323-329

Abstract

Multicentric clinical trials of the efficacy of Gugulipid conducted are reported. Two hundred and five patients completed 12 weeks open trial with gugulipid in a dose of 500 mg TDS after 8 weeks diet and placebo therapy.

A significant lowering of serum cholesterol (av. 23.6%) and serum triglycerides (av. 22.6%) was observed in 70-80% patients. Double-blind, cross over study was completed in 125 patients with gugulipid therapy and in 108 patients with clofibrate therapy. Two patients had flu like syndrome with clofibrate and opted out from the study. With the gugulipid, the average fall in serum cholesterol and triglycerides was 11 and 16.8% respectively and with clofibrate 10 and 21.6% respectively. The lipid lowering effect of both drugs become evident 3-4 weeks after starting the drug and had no relationship with age, sex and concomitant drug intake. Hypercholesterolemic patients responded better to gugulipid therapy than hypertriglyceridaemic patients who responded better to clofibrate therapy. In mixed hyperlipidaemic patients response to both drugs was comparable. HDL-cholesterol was increased in 60% cases who responded to gugulipid therapy. Clofibrate had no effect on HDL-cholesterol. A significant decrease in LDL-cholesterol was observed in the responder group to both drugs.

Comments

Fractions of gum guggul, the resin from commiphora mukul, were found to cause significant lowering of blood lipids and change in lipoprotein profile. Sterones present in the resin are responsible for the activity. One of fraction of resin named Gugulipid is almost as active as the pure sterones. It has also shown inhibition of platelet aggregation and a weak and-inflammatory activity. It inhibits cholesterol bioynthesis, has antilipolytic action and is devoid of any hormonal, CNS, cardiovascular or diuretic effects.

INSULIN AUTO ANTIBODIES IN NON-OBESE DIABETIC (NOD) MICE

Michel C, Boitard C, Bach. JF

Clin. Exp. Immunol. 1989, 75 : 457-460

Abstract

Anti-insulin autoantibodies (IAA) were detected in NOD mice using ELISA. The antibodies were detected as early as at 5 weeks of age, long before onset of clinically overt diabetes, especially in diabetes proned female mice. The anti-insulin specificity was verified by passage on affinity was verified by passage on affinity chromotography insulin columns and demonstration that the anti-insulin activity was located on the F $(ab')_2$ region of the immunoglobulins. The presence of anti-insulin antibodies in prediabetic NOD mice provides a unique possibility for studying their significance and their eventual pathogenic role in the development of IDDM.

Comments

This study demonstrated presence of IAA in NOD mice. The antibodies detected was considered autoantibodies since the mice had not received any exogenous insulin till that time. IAA were detected in 41% of non-diabetic NOD mice, 46% diabetic NOD Mice and 6.9% of control mice, with a statistically significant difference between NOD mice and 6.9% of control mice ($P < 0.001$).

IAA production could be secondary to aggression against beta cells by auto-immune process, directed against islet cell membrane antigens, resulting in release of particularly immunogenic insulin (or pro-insulin). They would then only represent a marker of beta cell destruction as suggested in humans using a radioimmuno-precipitation assay and possibly should be assessed whether IAA could serve as an useful maker for the prediabetic state.

DIABETIC MYOCARDIAL INFARCTION : INTERACTION OF DIABETES WITH OTHER PRE-INFARCTION RISK FACTORS

Singer DE, Moulton A W, Nathon DM

Diabetes 1989, 38 : 350-357

Abstract

To assess the effect of diabetes on outcome, after acute myocardial infarction (MI) a cohort of 228 Type II (non-insulin dependent diabetic patients who had sustained acute MI with a similar number of diabetic patients with MI has been compared Thirty day mortality was greater in the diabetic group (27 vs. 17%) However, diabetic patients were older and had more cardiovascular disease before MI. Analysis accounting for such baseline risk revealed a complex effect of diabetes. The relative risk (RR) of dying from MI due to diabetes was greatest among patients with lower baseline risk (RR 7.3) and least among those at highest baseline risk (RR 0.83). These affected were most striking with transmural MI, which was highly lethal for those with diabetes. Analyses with pulmonary oedema as the end-point support the significant risk conferred by diabetes and its interaction with baseline risk. Diabetes is risk factor for poor outcome after MI particularly among patients whose per-MI cardiovascular status otherwise appears normal.

Comment

Diabetes is clearly a risk factor for death after MI, even when accounting for age, prior congestive heart failure (CHF), prior MI and extent of MI. This study has substantiated the results of earlier studies but has also provided a new prospective on diabetic risk with MI. First the risk conferred by diabetes occurs primarily among patients with the best apparent baseline cardiovascular status, i.e. younger patients without prior CHF or MI. These factors which have a strong effect on increasing risk in non-diabetic patients, add little to the risk in diabetic patients. Second, the increased risk of dying with MI due to diabetes is seen most dramatically with transmural MI. Underlying cause for this is unknown. Probably diabetes produces a cardiomyopathy that may be sub-clinical in the unstressed state but becomes evident with large MIs.

Other significant observations of their study are :

1. Diabetic women did as well as diabetic men.
2. Diabetic patients did not have a disproportionate number of late hospital deaths.
3. The majority of diabetic patients with MI presented with chest pain. The proportion was same as with non-diabetic patients. However, a significantly larger fraction of diabetic MIs. were heralded by dyspnoea.

INVESTIGATIONS IN CHILDREN WHO WERE IN UTERO AT ONSET OF INSULIN DEPENDENT DIABETES IN THEIR MOTHERS

Buschaurd K, Kohl C, Pederson LH

Lancet 1, 1989; 811-814

Abstract

55 children who were in utero whem type I diabetes developed in their mothers were studied at a mean (SEM) age of 10.4 (0.6) years. Only 1 was diabetic. Biochemical and immunological indices, measured in 35 children, showed no evidence of beta cell dysfunction. Thus, the fetal beta cell seem to be unaffected by the mechanism that cause diabetes in their mothers.

Comments

Type I diabetes often has an abrupt onset during pregnancy. In their study, the diabetogenic process in the pregnant mother has not affected Beta cell of the fetus with one exception, and none of the children in our study had biochemical or immunological signs of beta cells dysfunction.

Exact cause of IDDM in humans is not known. Coxsackie virus B4, which is associated with Type 1 diabetes in humans, can cross the placenta. Immune system is also actively involved in the diabetogenic process-IgG, but not IgM, can cross placental behaviour.

If foetal response to the diabetogenic factors in the pregnant mother were to lead to disease in the child, at what age could this be associated ? Probably further follow up of further follow up of these children may give a clue.

METFORMIN IMPROVES PERIPHERAL BUT NOT HEPATIC INSULIN ACTION IN OBESE PATIENTS WITH TYPE II DIABETES

Hother-Nielson O, Schwitz O, Andergen PH

Acta Endocrinologia, 1989; 120 : 257-265

Abstract

Nine obese patients with Type II diabetes mellitus were examined in a double blind cross over study. Metformin 0.5 g thrice daily or placebo were given for 4 weeks. At the end of each period, fasting and day time postprandial values of plasma glucose, insulin, C-peptide and lactate were determined, and in vivo insulin action was assessed using the euglycaemic clamp in combination with (3-^{3}H) glucose trace technique. Metformin treatment significantly reduced mean day time plasma glucose levels (10.2 ± 1.2 vs. 11.4 ± 1.2 mmol/L, P < 0.01) without enhancing mean day time plasma insulin (43 ± 4 vs. 50 ± 7 mU/l, NS> or C-peptide levels (1.26 ± 0.12 vs. 1.38 ± 0.18 mmol/1, NS). Fasting plasma lactate was unchanged (1.57 ±0.16 vs. 1.44 ± 0.11 mmol/L NS), whereas mean day time plasma lactate concentrations were slightly increased (1.78±0.11 vs. 1.38±0.11 mmol/L, P <0.01). The clamp study revealed that metformin treatment was associated with an enhanced

insulin mediated glucose utilization (370 ±38 *vs.* 313±33 rag, m^{-2}, min^{-1}, P<0.001), whereas insulin mediated suppression of hepatic glucose production was unchanged Also basal glucose clearance was improved (61.0 ± 5.8 vs 50.6±2.8 ml, m^{-2}, min^{-2}, P<0.05), whereas basal hepatic glucose production was unchanged (81 ±6 Vs 77 ±4mg. nT'-min^{-1}, NS) Conclusions.

1. Metformin treatment in obese Type II diabetic patients reduces hyperglycaemia without changing the insulin secretion.
2. The improved glycaemic control during metformin treatment was associated with an enhanced insulin mediated glucose utilisation, presumably in skeletal muscles, whereas no effect could be demonstrated on hepatic glucose production.

Comments

Most patients with Type II diabetes mellitus are obese and have insulin resistance and insulin levels that, although higher than normal, are insufficient to overcome the degree of insulin resistance. This study demonstrated that in obese Type II diabetic patients, metformin significantly reduces hyper glycemia without increasing plasma insulin levels. The improved glycaemic control was associated with enhanced insulin stimulated glucose utilization in peripheral tissues, whereas insulin-mediated suppression of hepatic glucose production and increment in glucose concentrations after meals were unchanged.

Improved insulin-stimulated glucose utilization after metformin has been shown in both Type II and Type I diabetes. This improvement appears to be identical in Type II and Type I diabetes, suggesting that this action of metformin is independent of endogenous insulin secretion. Decreased glucose utilization in skeletal muscles has been estimated to be primarily responsible for the peripheral insulin resistance in Type II diabetes, it is likely that antihyperglycaemic effect of metformin is mediated via an effect on skeletal muscles.

Biguanide therapy has been associated with hyperlactatemia and even lactic acidosis, with metformin, however, the risk of lactic acidosis **is** much lower than with phenformin and almost all cases reported in the literature have been associated with known contradictions predominately renal impairments. In this study fasting, lactate levels were found to be unchanged, however, postprandial plasma lactate levels were slightly elevated.

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